

Please add the following new claim.

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--11. A pharmaceutical preparation, comprising,
a pharmacological acceptable salt of dichloromethylene bisphosphonic
acid, and
an excipient, said excipient comprising silicified microcrystalline
cellulose obtained by coprocessing microcrystalline cellulose with from about
0.1 to about 20% silicon dioxide, based on the amount of microcrystalline
cellulose.--

REMARKS

Claims 1-9 and 11 are pending in the present application. The "Abstract of the Disclosure" is the same as that found in the PCT International Application. Applicant has canceled claim 10. Original claim 1 and the specification on page 3, lines 20-28 provides basis for new claim 11. Applicant has not raised any issue of new matter.

Issues under 35 U.S.C. § 112 and § 101

Applicant has canceled claim 10. This action renders the 35 U.S.C. § 112 and § 101 rejections moot. Applicant respectfully requests withdrawal of the 35 U.S.C. § 112 and § 101 rejections.

Issue Under 35 U.S.C. § 102(b)

Claims 1-7 and 9-10 stand rejected under 35 U.S.C. §102(b) as being clearly anticipated by Posti '354 (USP 5,525,354). Applicant submits that patentable distinctions exist between the cited prior art and the present invention.

Present Invention

Applicant has directed the present invention to a pharmaceutical preparation for oral uses, especially tablet form, that has as its active ingredient a pharmacologically acceptable salt of dichloromethylene bisphosphonic acid and the excipient contains silicified microcrystalline cellulose. A second embodiment is a process for manufacture of the aforementioned pharmaceutical preparation.

The present invention solves many of the problems associated with the formulation of the drug clodronate. The prior art requires a very large oral dose of the active agent to reach an acceptable therapeutic activity. This requirement increases the size of the tablets; thus, reduces patient compliance.

Applicant uses silicified microcrystalline cellulose as an excipient, which has better powder flow and compactibility; thus, Applicant's tablet is stronger and smaller, which are advantages over the prior art.

Applicant obtains silicified microcrystalline cellulose as an excipient by coprocessing microcrystalline cellulose and silicon dioxide to form an

agglomerate of microcrystalline cellulose and silicon dioxide. This means that the silicon dioxide has been integrated with the microcrystalline cellulose, but no chemical interaction exists between the two components. *See page 3, lines 20-28.*

The clodronate preparations according to the present invention have a substantial reduction in tablet size; thus, an increase in patient compliance. Also, the production rate, in the case of the tablets, can be increased without adversely affecting the quality of the tablets. See Example 8, pages 10-11 of the present specification.

Distinctions Between the Present Invention and Posti '354

Posti '354 discloses a pharmaceutical preparation for oral use containing a pharmacologically acceptable salt of dichloromethylene bisphosphonic acid. Posti '354 discloses that the preparation may contain known carriers and other additives and adjuvants. Of these additives, Posti '354 discloses microcrystalline cellulose as a filler and colloidal silicon dioxide as a lubricant.

Posti '354 fails to disclose a pharmaceutical preparation containing silicified microcrystalline cellulose. The Examiner is correct that Example 1 does disclose that microcrystalline cellulose and colloidal silicon dioxide are present in the formulation as separate ingredients, but the Examiner is incorrect that Example 1 discloses silicified microcrystalline cellulose.

Applicant has defined silicified microcrystalline cellulose as the product of coprocessing microcrystalline cellulose with silicone dioxide. Posti '354 fails to disclose this material; Posti '354 only discloses that the individual ingredients are added to the preparation individually. Therefore, Posti '354 fails to disclose each element as set forth in the claims.

Applicant asserts that Posti '354 fails to anticipate the present invention. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Since Posti '354 fails to disclose an element of the present invention, Posti '354 fails to anticipate the present invention.

Applicant respectfully requests withdrawal of the 35 U.S.C. §102(b) rejection.

Issue Under 35 U.S.C. §103(a)

Claims 1-10 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Posti '354. Applicant submits the patentable distinctions exist between the cited prior art and the present invention.

Distinctions Between the Present Invention and Posti '354

The Examiner has asserted that Posti' 354 fails to disclose a process of dry granulation. However, the Examiner asserts that a skilled artisan would use dry granulation, because it is well known in the art.

As stated above, Posti '354 fails to disclose or suggest a pharmaceutical preparation containing dichloromethylene bisphosphonic acid, and silicified microcrystalline cellulose. Posti '354 fails to recognize the benefit of using silicified microcrystalline cellulose. Posti '354 fails to suggest an agglomerate of microcrystalline cellulose and silicone dioxide. Posti '354 uses microcrystalline cellulose and silicon dioxide separately, which is a traditional way to form a pharmaceutical preparation.

The Examiner must present a *prima facie* case of obviousness consisting of motivation or suggestion to modify or combine references such that one of ordinary skill in the art has a reasonable expectation of success of making the present composition. The cited reference fails to disclose or suggest each element as set forth in the claims; thus, a *prima facie* case of obviousness has not been presented.

Therefore, a patentable distinction exists between the present invention and the cited reference. Applicant respectfully requests withdrawal of the 35 U.S.C. § 103(a) rejection.

Conclusion

Applicant submits for the reasons stated above that the present claims define patentable subject matter such that this application should be placed into condition for allowance.

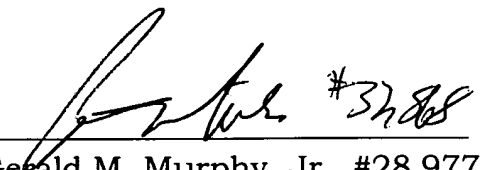
If the Examiner has any questions regarding the above matters, please contact Applicants' representative, Mark W. Milstead (Reg. No. 45,825), in the Washington, metropolitan area at the telephone number listed below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and further replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fee required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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